

IN THE SPECIFICATION:

Please replace the paragraph beginning on page 1, line 7 with the following amended paragraph:

Field of the invention

The present invention relates to the use of cyclophilin with peptidyl-propyl prolyl-cis-trans isomerase (PPIase) activity as an antioxidant and a method of preventing immunosuppressant cyclosporin A (CsA)-induced toxicity in cell transplantation by overexpressing cyclophilin.

Please replace paragraph beginning on page 1, line 13 with the following amended paragraph:

Brief Description of the Prior Art

CsA (Cyclosporin A) is a potent immunosuppressant that is widely used in organ transplantation and autoimmune diseases (Alejandro, D. S., et al., J. Am. Soc. Nephrol. 5, 153-160, 1994). CsA is a cyclic undecapeptide that bind to cyclophilin A (CypA) with a high affinity. CypA is a cytosolic protein with PPIase (peptidyl-propyl prolyl-cis-trans isomerase) activity that is potently inhibited by CsA binding. PPIase enzymes function as molecular chaperones to facilitate protein folding, intracellular trafficking and maintenance mult-protein complex stability (Andreeva, L., et al., Int. J. Exp. Pathol. 80, 305-315, 1999; Hamilton, G. S., et al., J. Med. Chem. 41, 5119-5143, 1998), although it is believed that inhibition of PPIase activity is not required for its immunosuppressive action (Bierer, B. E., et al., Science 250, 556-559, 1990). CsA-CypA complex, but not CypA alone, binds and inhibits the activity of calcineurin, which is a calcium/calmodulin-dependent protein phosphates. (Friedman, J., et al., Cell 66, 799-806, 1991; Liu, J., et al., Biochemistry 31, 3896-3901, 1992). The inhibitor of calcineurin activity blocks the translocation of NFATs (nuclear factors of activated T-cells), which in turn prevents T-helper cells from expressing several lymphokines that mediate the activation of immune reaction (Matsuda, S., et al., Immunopharmacology 47, 119-125, 2000).